

ITW

PTO/SB/21 (09-04)

Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

**TRANSMITTAL
FORM**

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

Application Number 10/574,167

Filing Date March 29, 2006

First Named Inventor BUSH et al.

Art Unit TBD

Examiner Name TBD

Attorney Docket Number 8028-007-US

ENCLOSURES (Check all that apply)

<input type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> After Allowance Communication to TC
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input type="checkbox"/> Amendment/Reply	<input type="checkbox"/> Petition	<input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
<input type="checkbox"/> After Final	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Proprietary Information
<input type="checkbox"/> Affidavits/declaration(s)	<input type="checkbox"/> Power of Attorney, Revocation	<input type="checkbox"/> Status Letter
<input type="checkbox"/> Extension of Time Request	<input type="checkbox"/> Change of Correspondence Address	<input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):
<input type="checkbox"/> Express Abandonment Request	<input type="checkbox"/> Terminal Disclaimer	- Copies of References Cited
<input checked="" type="checkbox"/> Information Disclosure Statement	<input type="checkbox"/> Request for Refund	- Self-Addressed, Stamped Postcard
<input type="checkbox"/> Certified Copy of Priority Document(s)	<input type="checkbox"/> CD, Number of CD(s) _____	
<input type="checkbox"/> Reply to Missing Parts/Incomplete Application	<input type="checkbox"/> Landscape Table on CD	
<input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53		

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	CATALYST LAW GROUP, APC		
Signature			
Printed name	Michael B. Farber, Ph.D., Esq.		
Date	June 8, 2006	Reg. No.	32,612

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature			
Typed or printed name	Sara Hare	Date	June 8, 2006

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



PATENT
8028-007-US

CERTIFICATE OF MAILING
(37 C.F.R. §1.8a)

I hereby certify that this paper (along with any referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as First Class Mail in an envelope addressed to the Commissioner for Patents, Mail Stop: Information Disclosure Statement, P. O. Box 1450, Alexandria, VA 22313-1450.

June 8, 2006
Date of Deposit

S. Hare
Signature of Person Mailing Paper

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)	Examiner: To Be Assigned
)	
Bush et al.)	Group Art Unit: To Be Assigned
)	
Serial No.: 10/547,176)	Docket No.: 8028-007-US
)	
Filed: March 29, 2006)	Date Mailed: June 8, 2006
)	
For: USE OF CELL LINES TO)	
PRODUCE ACTIVE THERAPEUTIC)	
PROTEINS)	

INFORMATION DISCLOSURE STATEMENT

Mail Stop: Information Disclosure Statement
Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This document is an Information Disclosure Statement to the above-cited patent application.

Attached is at least one form PTO/SB/08A/B listing documents believed relevant to the subject application. The submission of the following information is not intended, nor should it be construed, to constitute an admission that any patent, article, or other information referred to herein is "prior art" unless specifically designated as such. In accordance with 37 C.F.R. § 1.97(b), the filing of this information shall not be construed to mean that a search has been made or that no other material information may exist. Neither should its submission be construed to indicate that a thorough search should not be conducted by the Examiner.

It is believed that this disclosure complies with the requirements of 37 C.F.R. § 1.96, § 1.97, and § 1.98 and the Manual of Patent Examining Procedures § 707.05(b). If for some reason the Examiner considers otherwise, it is respectfully requested that the undersigned be telephoned at (858) 450-0099 x302 so that any deficiencies can be remedied.

This Information Disclosure Statement is being submitted within three months of the filing date of the above-identified patent application. Accordingly, no fee is due for the filing of this Information Disclosure Statement under 37 C.F.R. § 1.97(b)(1).

A copy of each document is enclosed, except for issued United States patents and published United States patent applications pursuant to 37 C.F.R. § 1.98(a)(2)(ii). Some of the documents may have markings thereon. No significance is to be attached to the markings. These documents are not necessarily analogous art. Additionally, the order of the following documents is to be accorded no particular import, as the order thereof is completely fortuitous.

It is respectfully requested that these documents be: (1) fully considered by the Patent and Trademark Office during the prosecution of this application; and (2) represented on any patent which may issue on the application. Applicant respectfully requests that copies of the forms PTO/SB/08A/B, as considered and initialed by the Examiner, be returned with the next communication.

U.S. Patent No. 5,665,589 to Harris et al., issued on September 9, 1997.

U.S. Patent No. 6,046,050 to Strauss et al., issued on April 4, 2000.

U.S. Patent No. 6,107,043 to Jauregui et al., issued on August 22, 2000.

U.S. Patent No. 6,517,830 to Lollar et al., issued on February 11, 2003.

U.S. Patent No. 6,806,351 to Ruben et al. issued on October 19, 2004.

U.S. Patent Application Publication No. 2002/0045262 by Prachumsri, published on April 18, 2002.

PCT Patent Application Publication No. WO 99/55853 by Fukaya et al., published on November 4, 1999, which describes a novel immortalized hepatic cell line originating in normal human (preferably human fetal) cells, a process for producing this cell line; a method for screening compounds or salts thereof capable of inhibiting or promoting the activity of an enzyme participating in the metabolism of a biological foreign matter in the liver, inhibiting or promoting the expression of a gene encoding an enzyme participating in the metabolism of a biological foreign matter in the liver, or inhibiting or promoting the induction of the expression of a gene encoding an enzyme participating in the metabolism of a biological foreign matter in the liver, the process involving using the above-mentioned cell line. The application further describes compounds capable of inhibiting or promoting the activity of an enzyme participating in the metabolism of a biological foreign matter in the liver, compounds capable of

inhibiting or promoting the expression of a gene encoding an enzyme participating in the metabolism of a biological foreign matter in the liver, compounds capable of inhibiting or promoting the induction of the expression of a gene encoding an enzyme participating in the metabolism of a biological foreign matter in the liver, or salts of these compounds obtained by the above screening method. The cell line is described as useful in, for example, screening compounds having preventive/therapeutic effects on liver failure.

A publication, J.B. Mills et al., "Induction of Drug Metabolism Enzymes and MDR1 Using a Novel Human Hepatocyte Cell Line," J. Pharm. Exp. Therap. 309: 303-309 (2003).

A publication, B.K. Lucas et al., "High-Level Production of Recombinant Proteins in CHO Cells Using a Dicistronic DHFR Intron Expression Vector," Nucleic Acids Res. 24: 1774-1779 (1996).

A publication, U. Janssen et al., "Expression of Inter- α -Trypsin Inhibitor and Tumor Necrosis Factor-Stimulated Gene 6 in Renal Proximal Tubular Epithelial Cells," Kidney Int'l 60: 126-136 (2001).

A publication, J. Collinge et al., "Molecular Analysis of Prion Strain Variation and the Aetiology of "New Variant" CJD," Nature 383: 685-690 (1996).

A publication, C.G. White et al., "Recombinant Factor IX," Thromb. Haemost. 78: 261-265 (1997).

A publication, J.M. Soucie et al., "Hemophilia Occurrence in the United States," Am. J. Hematol. 59: 288-294 (1998).

A publication, J.P. Salier et al., "The Inter- α -Inhibitor Family: From Structure to Regulation," Biochem. J. 351: 1-9 (1996).

A publication, J. Ludlow, "Interactions Between SV40 Large-Tumor Antigen and the Growth Suppressor Proteins pRB and p53," *FASEB J.* 7: 866-871 (1993).

A publication, M. Popovic et al., "Transformation of Human Umbilical Cord Blood T-Cells by Human T-Cell Leukemia/Lymphoma Virus (HTLV)," *Proc. Natl. Acad. Sci. USA* 80:5402-5406 (1983).

A publication, A.S. Nies & S.P. Spielberg, "Principles of Therapeutics" in J.G. Hardman & L.E. Limbird, eds., "Goodman & Gilman's The Pharmacological Basis of Therapeutics" (9th ed., McGraw-Hill, New York, 1996), ch. 3., pp. 43-62.

A publication, Zola et al., in *Monoclonal Hybridoma Antibodies: Techniques and Applications* (Hurell, ed., CRC Press, 1982), pp. 51-52.

A publication, J. Rousseaux et al., "Optimal Conditions for the Preparation of Proteolytic Fragments from Monoclonal IgG of Different Rat IgG Subclasses" *Methods Enzymol.*, 121:663-69 (1986).

A publication, M. K. Paterson, "Measurement of Growth and Viability of Cells in Culture" *Methods Enzymol.* 58:141 (1979).

A publication, L.H. Thompson, "Mutant Isolation" *Methods Enzymol.* 58: 308 (1979).

A publication, Grynkiewicz et al, "A New Generation of Ca²⁺ Indicators with Greatly Improved Fluorescence Properties" *J. Biol. Chem.* 260:3440-3450 (1985).

A publication, T. Tsurimoto et al, "Stable Expression and Replication of Hepatitis B Virus Genome in an Integrated State," *Proc. Natl. Acad. Sci. USA* 84:444-448 (1987).

A publication, Y.P. Lim et al., "Correlation Between Mortality and the Levels of Inter-alpha Inhibitors in Plasma of Severely Septic Patients," J. Infect. Dis. 188:919-926 (2003).

A publication, R. Levy et al., Metabolic Drug Interactions (Lippincott, William & Wilkins, Philadelphia, PA, 2000), pp. 3-19, 51-214.

A publication, T.D. Bjorsson et al., "The Conduct of in Vitro and in Vivo Drug-Drug Interaction Studies: A PhRMA Perspective," J. Clin. Pharmacol. 43: 443-469 (2003).

A publication, A. Madan et al., "Effects of Prototypical Microsomal Enzyme Inducers on Cytochrome P450 Expression in Cultured Human Hepatocytes," Drug Metab. Dispos. 31: 421-431 (2003).

A publication, E. LeCluyse et al., "Cultured Rat Hepatocytes" in Models for Assessing Drug Absorption and Metabolism (R.T. Borchard et al., eds., P.L Smith & G. Wilson, Plenum Press, New York, 1996), ch. 9., pp. 121-160.

A publication, E. LeCluyse et al., "Strategies for Restoration and Maintenance of Normal Hepatic Structure and Function in Long-Term Cultures of Rat Hepatocytes," Adv. Drug Delivery Rev. 22: 133-186 (1996).

A publication, D. Mudra & A. Parkinson, "Preparation of Hepatocytes for Drug Metabolism Studies" in Current Protocols in Toxicology Unit 5.8. (M Maines et al., eds., John Wiley & Sons, Inc. 2001), Unit 5.8.

A publication, A. Madan et al., "Effect of Cryopreservation on Cytochrome P450 Enzyme Induction in Cultured Rat Hepatocytes," Drug Metab. Dispos. 27: 327-335 (1999).

A publication, E. LeCluyse et al., "Influence of Extracellular Matrix Overlay and Medium Formulation on the Induction of Cytochrome P450 2B in Primary Cultures of Rat Hepatocytes," *Drug Metab. Dispos.* 27: 909-915 (1999).

A publication, E. LeCluyse et al., "Expression and Regulation of Cytochrome P450 Enzymes in Primary Cultures of Human Hepatocytes," *J. Biochem. Mol. Toxicol.* 14: 177-188 (2000).

A publication, Luo et al., "CYP3A4 Induction by Drugs: Correlation Between a Pregnane X Receptor Reporter Gene Assay and CYP3A4 Expression in Human Hepatocytes," *Drug Metab. Dispos.* 30: 795-804 (2002).

A publication, A. Abid et al., "Expression and Inducibility of UDPglucuronyltransferases by 1-Naphthol in Human Cultured Hepatocytes and Hepatocarcinoma Cell Lines," *Life Sci.* 60: 1943-1951 (1997).

A publication, A.M. Baciewicz et al., "Update on Rifampin Drug Interactions," *Arch. Intern. Med.* 147: 565-568 (1987).

A publication, G. Bertilsson et al., (1998) "Identification of a Human Nuclear Receptor Defines a New Signaling Pathway for CYP3A Induction," *Proc. Natl. Acad. Sci. USA* 95: 12208-12213 (1998).

A publication, M.D. Burke et al., "Ethoxy-, Pentoxy- and Benzyloxyphenoxazones and Homologues: A Series of Substrates to Distinguish Between Different Induced Cytochromes P-450," *Biochem. Pharmacol.* 34: 3337-3345 (1985).

A publication, P.S. Eis et al., "An Invasive Cleavage Assay for Direct Quantitation of Specific RNAs," *Nature Biotechnol.* 19: 673-676 (2001).

A publication, S.S. Ferguson et al., "Regulation of Human CYP2C9 by the Constitutive Androstane Receptor: Discovery of a New Distal Binding Site," *Mol. Pharmacol.* 62: 737-746 (2002).

A publication, A. Geick et al., "Nuclear Receptor Response Elements Mediate Induction of Intestinal MDR1 by Rifampin," *J. Biol. Chem.* 276: 14581-14587 (2001).

A publication, T. Leemann et al., "Cytochrome P450TB (CYP2C): A Major Monooxygenase Catalyzing Diclofenac 4'-Hydroxylation in Human Liver," *Life Sci.* 52: 29-34 (1993).

A publication, J.M. Lehmann et al. "The Human Orphan Nuclear Receptor PXR is Activated by Compounds that Regulate CYP3A4 Gene Expression and Cause Drug Interactions," *J. Clin. Invest.* 102: 1016-1023 (1998).

A publication, A.P. Li et al., "Primary Human Hepatocytes as a Tool for the Evaluation of Structure-Activity Relationship in Cytochrome P450 Induction Potential of Xenobiotics: Evaluation of Rifampin, Rifapentine and Rifabutin," *Chem. Biol. Interact.* 107: 17-30 (1997).

A publication, W. Li et al., "Regulation of Cytochrome P450 Enzymes by Aryl Hydrocarbon Receptor in Human Cells," *Biochem. Pharmacol.* 56: 599-612 (1998).

J.M Pascussi et al., "The Expression of CYP2B6, CYP2C9 and CYP3A4 Genes: A Tangle of Networks of Nuclear and Steroid Receptors," *Biochim. Biophys. Acta* 1619: 243-253 (2003).

A publication, A.D. Rodrigues & R.A. Prough RA, "Induction of Cytochromes P450IA1 and P450IA2 and Measurement of Catalytic Activities," *Methods Enzymol.* 206: 423-431 (1991).

A publication, J. Sahi et al., "Avasimibe Induces CYP3A4 and Multiple Drug Resistance Protein 1 Gene Expression Through Activation of the Pregnane X Receptor," J. Pharmacol. Exp. Ther. 306: 1027-1034 (2003).

A publication, E.G. Schuetz et al., "Modulators and Substrates of P-Glycoprotein and Cytochrome P4503A Coordinately Up-Regulate These Proteins in Human Colon Carcinoma Cells," Mol. Pharmacol. (49): 311-318 (1996).

A publication, A.J. Sonderfan et al., "Regulation of Testosterone Hydroxylation by Rat Liver Microsomal Cytochrome P-450," Arch. Biochem. Biophys. 255: 27-41 (1987).

A publication, A.J. Sonderfan & A. Parkinson, "Inhibition of Steroid 5 Alpha-Reductase and Its Effects on Testosterone Hydroxylation by Rat Liver Microsomal Cytochrome P-450," Arch. Biochem. Biophys. 265: 208-218 (1988).

A publication, E. Spina et al., "Clinically Significant Pharmacokinetic Drug Interactions with Carbamazepine: An Update," Clin. Pharmacokinet. 31: 198-214 (1996).

A publication, R.G. Tirona et al., "Human Organic Anion Transporting Polypeptide-C (SLC21A6) Is a Major Determinant of Rifampin-Mediated Pregnane X Receptor Activation," J. Pharmacol. Exp. Ther. 304: 223-228 (2003).

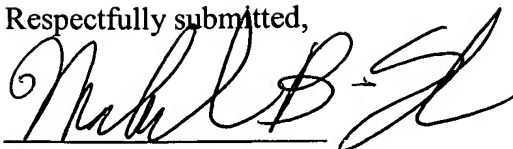
A publication, J.P. Whitlock et al., "Induction of Cytochrome P4501A1: A Model for Analyzing Mammalian Gene Transcription," FASEB 10: 809-818 (1996).

A publication, A.J. Williams et al., "Comparative Metabolic Capabilities of CYP3A4, CYP3A5, and CYP3A7," Drug Metab. Dispos. 30: 883-891(2002).

A publication, A.W. Wood et al., "Regio- and Stereoselective Metabolism of two C19 Steroids by Five Highly Purified and Reconstituted Rat Hepatic Cytochrome P-450 Isozymes," J. Biol. Chem. 258: 8839-8847 (1983).

Date: June 8, 2006

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Michael B. Farber", written over a horizontal line.

Michael B. Farber, Ph.D., Esq.
Reg. No.: 32,612

CATALYST LAW GROUP, APC
9710 Scranton Road, Suite 170
San Diego, California 92121
(858) 450-0099
(858) 450-9834 (Fax)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet

1

of

T

Complete if Known

Application Number	10/574 167
--------------------	------------

Filing Date	March 29, 2006
-------------	----------------

First Named Inventor	BUSH et al.
----------------------	-------------

Art Unit	TBD
----------	-----

Examiner Name	TBD
---------------	-----

Attorney Docket Number	8028-007-US
------------------------	-------------

U. S. PATENT DOCUMENTS

[illegible]

FOREIGN PATENT DOCUMENTS

[illegible]

**Examiner
Signature**

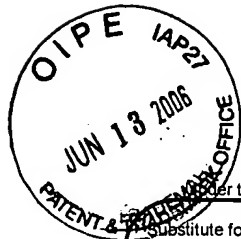
Date _____

Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.



PTO/SB/08B (07-05)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.
Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Complete if Known

Application Number	10/574,167
Filing Date	March 29, 2006
First Named Inventor	BUSH et al.
Art Unit	TBD
Examiner Name	TBD
Attorney Docket Number	8028-007-US

Sheet 1 of 5

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		J.B. MILLS et al., "Induction of Drug Metabolism Enzymes and MDR1 Using a Novel Human Hepatocyte Cell Line," J. Pharm. Exp. Therap. 309: 303-309 (2003).	
		B.K. LUCAS et al., "High-Level Production of Recombinant Proteins in CHO Cells Using a Dicistronic DHFR Intron Expression Vector," Nucleic Acids Res. 24: 1774-1779 (1996).	
		U. JANSSEN et al., "Expression of Inter- α -Trypsin Inhibitor and Tumor Necrosis Factor-Stimulated Gene 6 in Renal Proximal Tubular...", Kidney Int'l 60: 126-136 (2001).	
		J. COLLINGE et al., "Molecular Analysis of Prion Strain Variation and the Aetiology of "New Variant" CJD," Nature 383: 685-690 (1996).	
		C.G. WHITE et al., "Recombinant Factor IX," Thromb. Haemost. 78: 261-265 (1997).	
		J.M. SOURCIE et al., "Hemophilia Occurrence in the United States," Am. J. Hematol. 59: 288-294 (1998).	
		J.P. SALIER et al., "The Inter- α -Inhibitor Family: From Structure to Regulation," Biochem. J. 351: 1-9 (1996).	
		J. LUDLOW, "Interactions Between SV40 Large-Tumor Antigen and the Growth Suppressor Proteins pRB and p53," FASEB J. 7: 866-871 (1993).	
		M. POPOVIC et al., "Transformation of Human Umbilical Cord Blood T-Cells by Human T-Cell Leukemia/Lymphoma Virus (HTLV)," Proc. Natl. Acad. Sci. USA 80:5402-5406 (1983).	
		A.S. NIES & S.P. SPIELBERG, "Principles of Therapeutics" in J.G. Hardman & L.E. Limbird, eds., "Goodman &...", (9th ed., McGraw-Hill, New York, 1996), ch. 3., pp. 43-62.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>		Complete if Known			
		Application Number	10/574,167		
		Filing Date	March 29, 2006		
		First Named Inventor	BUSH et al.		
		Art Unit	TBD		
		Examiner Name	TBD		
Sheet	2	of	5	Attorney Docket Number	8028-007-US

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		ZOLA et al., in Monoclonal Hybridoma Antibodies: Techniques and Applications (Hurell, ed., CRC Press, 1982), pp. 51-52.	
		J. ROUSSEAU et al., "Optimal Conditions for the Preparation of Proteolytic Fragments from Monoclonal IgG of Different Rat IgG Subclasses" Methods Enzymol., 121:663-69 (1986).	
		M. K. PATERSON, "Measurement of Growth and Viability of Cells in Culture" Methods Enzymol. 58:141 (1979).	
		L.H. THOMPSON, "Mutant Isolation" Methods Enzymol. 58: 308 (1979).	
		GRYNKIEWICZ et al, "A New Generation of Ca ²⁺ Indicators with Greatly Improved Fluorescence Properties" J. Biol. Chem. 260:3440-3450 (1985).	
		T. TSURIMOTO et al, "Stable Expression and Replication of Hepatitis B Virus Genome in an Integrated State," Proc. Natl. Acad. Sci. USA 84:444-448 (1987).	
		Y.P. LIM et al., "Correlation Between Mortality and the Levels of Inter-alpha Inhibitors in Plasma of Severely Septic Patients," J. Infect. Dis. 188:919-926 (2003).	
		R. LEVY et al., Metabolic Drug Interactions (Lippincott, William & Wilkins, Philadelphia, PA, 2000), pp. 3-19, 51-214.	
		T.D. BJORSSON et al., "The Conduct of in Vitro and in Vivo Drug-Drug Interaction Studies: A PhRMA Perspective," J. Clin. Pharmacol. 43: 443-469 (2003).	
		A. MADAN et al., "Effects of Prototypical Microsomal Enzyme Inducers on Cytochrome P450 Expression in Cultured Human Hepatocytes," Drug Metab. Dispos. 31: 421-431 (2003).	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>		Complete if Known	
		Application Number	10/574,167
		Filing Date	March 29, 2006
		First Named Inventor	BUSH et al.
		Art Unit	TBD
		Examiner Name	TBD
Sheet	3	of	5
		Attorney Docket Number	8028-007-US

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		E. LECLUYSE et al., "Cultured Rat Hepatocytes" in Models for..., (R.T. Borchard et al., eds., P.L Smith & G. Wilson, Plenum Press, New York, 1996), ch. 9., pp. 121-160.	
		E. LECLUYSE et al., "Strategies for Restoration and Maintenance of Normal Hepatic Structure and Function in Long-Term Cultures...", Adv. Drug Delivery Rev. 22: 133-186 (1996).	
		D. MUDRA & A. PARKSINSON, "Preparation of Hepatocytes for...", in Current Protocols in Toxicology Unit 5.8. (M Maines et al., eds., John Wiley & Sons, Inc. 2001), Unit 5.8.	
		A. MADAN et al., "Effect of Cryopreservation on Cytochrome P450 Enzyme Induction in Cultured Rat Hepatocytes," Drug Metab. Dispos. 27: 327-335 (1999).	
		E. LECLUYSE et al., "Influence of Extracellular Matrix Overlay and Medium Formulation on the Induction of Cytochrome P450 2B in...", Drug Metab. Dispos. 27: 909-915 (1999).	
		E. LECLUYSE et al., "Expression and Regulation of Cytochrome P450 Enzymes in Primary Cultures of Human Hepatocytes," J. Biochem. Mol. Toxicol. 14: 177-188 (2000).	
		LUO et al., "CYP3A4 Induction by Drugs: Correlation Between a Pregnane X Receptor Reporter Gene Assay and CYP3A4...", Drug Metab. Dispos. 30: 795-804 (2002).	
		A. ABID et al., "Expression and Inducibility of UDPglucuronyltransferases by 1-Naphthol in Human Cultured Hepatocytes and Hepatocarcinoma...", Life Sci. 60: 1943-1951 (1997).	
		A.M. BACIEWICZ et al., "Update on Rifampin Drug Interactions," Arch. Intern. Med. 147: 565-568 (1987).	
		G. BERTILSSON et al., (1998) "Identification of a Human Nuclear Receptor Defines a New Signaling Pathway for CYP3A...", Proc. Natl. Acad. Sci. USA 95: 12208-12213 (1998).	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>		Complete if Known	
		Application Number	10/574,167
		Filing Date	March 29, 2006
		First Named Inventor	BUSH et al.
		Art Unit	TBD
		Examiner Name	TBD
		Attorney Docket Number	8028-007-US
Sheet	4	of	5

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		M.D. BURKE et al., "Ethoxy-, Pentoxy- and Benzyloxyphenoxazones and Homologues: A Series of Substrates to Distinguish Between...", Biochem. Pharmacol. 34: 3337-3345 (1985).	
		P.S. EIS et al., "An Invasive Cleavage Assay for Direct Quantitation of Specific RNAs," Nature Biotechnol. 19: 673-676 (2001).	
		S.S. FERGUSON et al., "Regulation of Human CYP2C9 by the Constitutive Androstane Receptor: Discovery of a New Distal Binding Site," Mol. Pharmacol. 62: 737-746 (2002).	
		A. GEICK et al., "Nuclear Receptor Response Elements Mediate Induction of Intestinal MDR1 by Rifampin," J. Biol. Chem. 276: 14581-14587 (2001).	
		T. LEEMANN et al., "Cytochrome P450TB (CYP2C): A Major Monooxygenase Catalyzing Diclofenac 4'-Hydroxylation in Human Liver," Life Sci. 52: 29-34 (1993).	
		J.M. LEHMANN et al. "The Human Orphan Nuclear Receptor PXR is Activated by Compounds that Regulate CYP3A4 Gene Expression and...", J. Clin. Invest. 102: 1016-1023 (1998).	
		A.P. LI et al., "Primary Human Hepatocytes as a Tool for the Evaluation of Structure-Activity Relationship in Cytochrome P450...", Chem. Biol. Interact. 107: 17-30 (1997).	
		W. LI et al., "Regulation of Cytochrome P450 Enzymes by Aryl Hydrocarbon Receptor in Human Cells," Biochem. Pharmacol. 56: 599-612 (1998).	
		J.M. PASCUSI et al., "The Expression of CYP2B6, CYP2C9 and CYP3A4 Genes: A Tangle of Networks of Nuclear and Steroid Receptors," Biochim. Biophys. Acta 1619: 243-253 (2003).	
		A.D. RODRIGUES & R.A. PROUGH RA, "Induction of Cytochromes P450IA1 and P450IA2 and Measurement of Catalytic Activities," Methods Enzymol. 206: 423-431 (1991).	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>		Complete if Known	
		Application Number	10/574,167
		Filing Date	March 29, 2006
		First Named Inventor	BUSH et al.
		Art Unit	TBD
		Examiner Name	TBD
		Attorney Docket Number	8028-007-US
Sheet	5	of	5

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		J. SAHI et al., "Avasimibe Induces CYP3A4 and Multiple Drug Resistance Protein 1 Gene Expression Through Activation...", J. Pharmacol. Exp. Ther. 306: 1027-1034 (2003).	
		E.G. SCHUETZ et al., "Modulators and Substrates of P-Glycoprotein and Cytochrome P4503A Coordinately Up-Regulate These Proteins...", Mol. Pharmacol. (49): 311-318 (1996).	
		A.J. SONDERFAN et al., "Regulation of Testosterone Hydroxylation by Rat Liver Microsomal Cytochrome P-450," Arch. Biochem. Biophys. 255: 27-41 (1987).	
		A.J. SONDERFAN & A. PARKINSON, "Inhibition of Steroid 5 Alpha-Reductase and Its Effects on Testosterone Hydroxylation by Rat...", Biochem. Biophys. 265: 208-218 (1988).	
		E. SPINA et al., "Clinically Significant Pharmacokinetic Drug Interactions with Carbamazepine: An Update," Clin. Pharmacokinet. 31: 198-214 (1996).	
		R.G. TIRONA et al., "Human Organic Anion Transporting Polypeptide-C (SLC21A6) Is a Major Determinant of Rifampin-Mediated...", J. Pharmacol. Exp. Ther. 304: 223-228 (2003).	
		J.P. WHITLOCK et al., "Induction of Cytochrome P4501A1: A Model for Analyzing Mammalian Gene Transcription," FASEB 10: 809-818 (1996).	
		A.J. WILLIAMS et al., "Comparative Metabolic Capabilities of CYP3A4, CYP3A5, and CYP3A7," Drug Metab. Dispos. 30: 883-891(2002).	
		A.W. Wood et al., "Regio- and Stereoselective Metabolism of two C19 Steroids by Five Highly Purified and Reconstituted Rat...", J. Biol. Chem. 258: 8839-8847 (1983).	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.